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(54) Preparation of esters containing an alpha cyano group in the alcohol portion of the ester.

(57) Alpha-cyano esters are prepared by reacting an acyl halide with an aldehyde in a substantially water-immiscible aprotic solvent and an aqueous solution of water-soluble cyanide salt in the presence of tertiary amine or polyamine, cryptate, amphoteric surfactant or acid salt of tertiary amine rate-promoting agent.

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PREPARATION OF ESTERS

This invention relates to a process for preparing esters of carboxylic acids, more specifically, esters which contain a cyano group bonded to the alpha-carbon atom in the alcohol portion of the ester molecule.

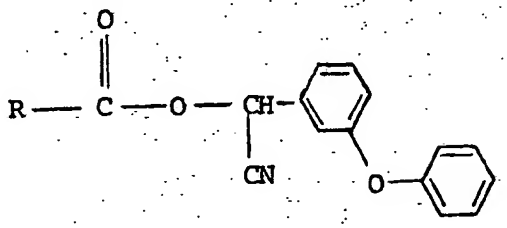
Esters with a cyano group so situated are prepared by reacting an acid with the appropriate cyanohydrin. According to U.S. 3,835,176, the reaction can also be effected by treating an acyl halide with a mixture of the appropriate aldehyde and aqueous sodium or potassium cyanide, optionally in an aprotic solvent. It is disclosed, for example, that 3-phenoxy-α-cyanobenzyl chrysanthemate is prepared in 64% yield by reacting chrysanthemoyl chloride, 3-phenoxybenzaldehyde, and an aqueous solution of sodium cyanide at 0°C for 1 hour.

Were it possible to shorten the reaction time and increase the yield, producing this and other alpha-cyano esters by reacting an acyl halide with an aldehyde and a cyanide would be of great commercial interest. Insecticidal alpha-cyano esters whose preparations would be facilitated include α-cyano-3-phenoxybenzyl 3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropanecarboxylate and α-cyano-3-phenoxybenzyl 3-(2,2-dibromoethenyl)-2,2-dimethylcyclopropanecarboxylate. Other insecticidal alpha-cyano esters of particular interest are α-cyano-3-phenoxybenzyl 3-(2-chloro-3,3,3-trifluoropropenyl)2,2-dimethylcyclopropanecarboxylate, α-cyano-3-phenoxybenzyl 2,2,3,3-tetramethylcyclopropanecarboxylate, and α-cyano-3-phenoxybenzyl 2-(4-chlorophenyl)-3-methylbutanoate.

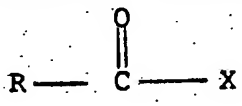
One advantage of this invention is that it provides a process for making alpha-cyano esters in very high yield in a short time. Another advantage of this invention is that it provides an esterification process whose product does not require lengthy and expensive purification.

Accordingly, this invention provides a process to prepare an alpha-cyano ester by reacting an acyl halide with an aldehyde in a mixture of substantially water-immiscible aprotic solvent and an aqueous solution of water-soluble cyanide salt in the presence of a catalytic amount of rate-promoting agent selected from tertiary amines, polyamines, cryptates, amphoteric surfactants, and acid-salts of tertiary amines. Either the acyl halide or the aldehyde may exhibit optical or geometric isomerism, which is not affected by the reaction.

In a preferred embodiment, there is provided a process for preparing an insecticidal α-cyano-3-phenoxybenzyl ester of the formula



wherein R is selected from 3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropyl, 3-(2,2-dibromoethenyl)-2,2-dimethylcyclopropyl, 3-(2-chloro-3,3,3-trifluoropropenyl)-2,2-dimethylcyclopropyl, 2,2,3,3-tetramethylcyclopropyl, and 1-(4-chlorophenyl)-2-methylpropyl which comprises reacting an acyl halide of the formula

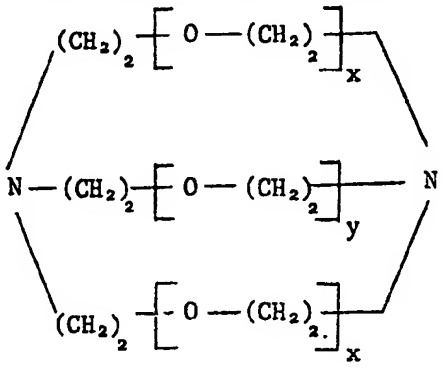


wherein X is chlorine or bromine and R is as defined above with 3-phenoxybenzaldehyde in a mixture of substantially water-immiscible aprotic solvent and an aqueous solution of water-soluble cyanide salt in the presence of a catalytic amount of rate-promoting agent selected from tertiary polyamines, cryptates, amphoteric surfactants selected from aminoalkylsulfonic acids, and acid salts of tertiary amines.

diazaoctane, or 2,5,8,11-tetramethyl-2,5,8,11-tetraazadecane.

6. The process of claim 5 characterized in that the rate promoting agent is diazabicyclo[2.2.2]octane.

7. The process of claim 3 characterized in that the rate promoting agent is a cryptate of the formula



wherein x and y are independently 1 or 2.

8. The process of claim 7 characterized in that the cryptate is 4,7,13,16,21-pentaoxo-1,10-diazabicyclo-[8.8.5]tricosane.

9. A process according to any one of claims 3-8 characterized in that R is 3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropyl.

10. A process according to any one of claims 3-8 characterized in that the water-immiscible aprotic solvent is n-heptane.

11. A process according to any one of claims 3-8 characterized in that the water-soluble cyanide salt is sodium cyanide.

12. The process of claim 2 characterized in that the rate-promoting agent is an aminoalkylsulfonic acid selected from 1,4-piperazinebisethanesulfonic acid, 4-pyridineethanesulfonic acid, 2-[N,N-di-(2-hydroxy)-ethyl]aminoethanesulfonic acid, 3-(cyclohexylamino)propanesulfonic acid, and 2-[4-(2-hydroxyethyl)piperizine-1-yl]ethanesulfonic acid.

13. The process of claim 12 characterized in that the rate-promoting agent is selected from 1,4-piperizine-bisethanesulfonic acid and 3-(cyclohexylamino)propane-

sulfonic acid.

14. The process of claim 13 characterized in that the rate-promoting agent is 3-(cyclohexylamino)propane-sulfonic acid.

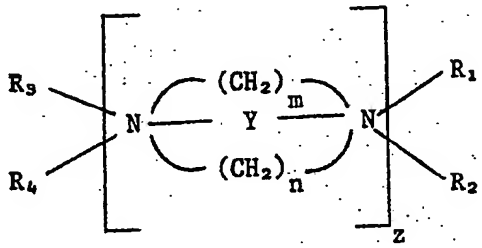
15. A process according to any one of claims 12-14 characterized in that R is 3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropyl or 1-(4-chlorophenyl)-2-methylpropyl.

16. A process according to any one of claims 12-14 characterized in that R is 3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropyl.

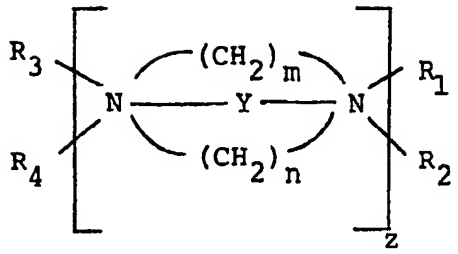
17. A process according to any one of claims 12-14 characterized in that the water-immiscible aprotic solvent is n-heptane.

18. A process according to any one of claims 12-14 characterized in that the water-soluble cyanide salt is sodium cyanide.

19. The process of claim 2 characterized in that the rate-promoting agent is an acid salt of a tertiary amine selected from products of the reaction of a strong acid and a linear tertiary polyamine of the formula



wherein Y is $-(CH_2)_k-$ with k being 1-6, C_3-C_7 cycloalkane, C_2-C_6 alkenyl, or C_2-C_6 alkynyl; z is 1 or 2, and when z is 1, m and n are 0 or independently 1-6, and when m and n are 0, R_1, R_2, R_3, and R_4 are hydrocarbon groups, and R_1 may be joined with R_2, and R_3 may be joined with R_4 to form a ring containing the N atom to which both are joined, and when m is 1-6 and n is 0, R_1 and R_3 are absent, and R_2 and R_4 are hydrocarbon groups, and when both m and n

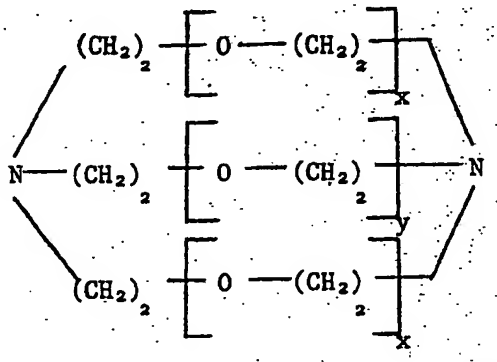


wherein Y is $-(CH_2)_k-$ with k being 1-6, C_3-C_7 cycloalkane, C_2-C_6 alkenyl, or C_2-C_6 alkynyl; z is 1 or 2, and when z is 1, m and n are 0 or independently 1-6, and when m and n are 0, R_1, R_2, R_3, and R_4 are hydrocarbon groups, and R_1 may be joined with R_2, and R_3 may be joined with R_4 to form a ring containing the N atom to which both are joined, and when m is 1-6 and n is 0, R_1 and R_3 are absent, and R_2 and R_4 are hydrocarbon groups, and when both m and n are at least 1, R_2 and R_4 are absent; and when z is 2, m and n are 0, R_1 and R_3 are hydrocarbon groups and R_2 and R_4 are absent.

Particularly useful linear tertiary polyamines within the aforesaid description are 2,4-dimethyl-2,4-diazapentane, 2,5-dimethyl-2,5-diazahexane, 1,1'-(1,2-ethanediyl)bis[piperidine], N,N,N',N'-tetramethyl-1,2-diaminocyclohexane, 1,4-dimethyl-1,4-diazacyclohexane, diazabicyclo[2.2.2]octane, 2,6-dimethyl-2,6-diazaheptane, 2,7-dimethyl-2,7-diazaoctane, 2,7-dimethyl-2,7-diaza-4-octene, 2,7-dimethyl-2,7-diaza-4-octyne, 2,9-dimethyl-2,9-diazadecane, and 2,5,8,11-tetramethyl-2,5,8, 11-tetraazadodecane. Among these compounds, diazabicyclo-[2.2.2]octane, 2,6-dimethyl-2,6-diazaheptane, 2,7-dimethyl-2,7-diazaoctane, and 2,5,8,11-tetramethyl-2,5,8,11-tetrazadecane are preferred, and diazabicyclo-[2.2.2]octane is especially attractive.

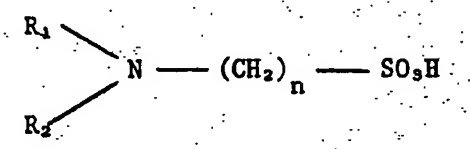
Macrocyclic tertiary polyamines such as 1,4,8,11-tetraazacyclotetradecane, for example, are also useful, as are sparteine and hexamethylenetetraamine.

Cryptates, polyoxadiazamacrobicycles, constitute another class of rate-promoting agent useful in the practice of this invention. Cryptates of the formula



wherein x and y are independently 1 or 2 are especially useful. When the cyanide salt is sodium cyanide 4,7,13, 16,21-pentaoxa-1,10-diazabicyclo[8.8.5]tricosane is preferred, but when lithium cyanide is employed 4,7,13, 18-tetraoxa-1,10-diazabicyclo[8.5.5]eicosane should be used, and 4,7,13,16,21, 24-hexaoxy-1,10-diazabicyclo-[8.8.8]hexacosane is preferred when potassium cyanide is employed.

Further, for purposes of this invention and wherever it appears in the specification or claims, the term "aminoalkylsulfonic acids", means compounds having the structural formula

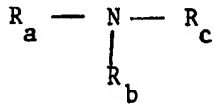


wherein n is 2 or 3, and wherein R_1 and R_2 are substituents selected collectively to render the aminoalkylsulfonic acids soluble in water-immiscible aprotic solvents. Suitable substituent groups, which collectively contain hydrocarbon units, are present in the following specific aminoalkylsulfonic acids: 1,4-piperazinebisethanesulfonic acid, 4-pyridineethanesulfonic acid, 2-[N,N-di-(2-hydroxy)ethyl]aminoethanesulfonic acid,

3-(cyclohexylamino)propanesulfonic acid, 2-[4-(2-hydroxyethyl)piperizine-1-yl]ethanesulfonic acid, 2-(N-morpholino)ethanesulfonic acid, N-tris(hydroxymethyl)methyl-2-aminoethanesulfonic acid, 2-(N-morpholino)propanesulfonic acid, and N-tris(hydroxymethyl)methyl-2-aminoethanesulfonic acid. Among these compounds, 1,4-piperizinebisethanesulfonic acid and 3-(cyclohexylamino)propanesulfonic acid are preferred, and 3-(cyclohexylamino)-propanesulfonic acid is especially effective.

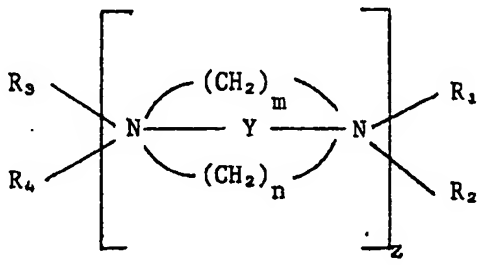
The tertiary amines whose acid salts are rate-promoting agents contain one or more, e.g., two, nitrogen atoms. For purposes of this invention and wherever it appears in the specification or claims the term, "acid salts of tertiary amines," means products of the reaction between a strong acid, such as HCl, HBr, H_2SO_4, HBF_4, $HClO_4$, or HCN and a tertiary amine or polyamine, a tertiary polyamine being a compound containing more than one tertiary amino nitrogen atom.

For purposes of this invention, a tertiary amine has the structural formula



wherein R_a, R_b, and R_c are hydrocarbon groups.

Particularly desirable tertiary polyamines within the scope of this invention are linear tertiary polyamines of the formula



wherein Y is $-(CH_2)_k-$ with k being 1-6, C_3-C_7 cycloalkane, C_2-C_6 alkenyl, or C_2-C_6 alkynyl; z is 1 or 2, and when z is 1, m and n are 0 or independently 1-6, and when m and n are 0, R_1, R_2, R_3, and R_4 are hydrocarbon groups, and R_1 may be joined with R_2, and R_3 may be joined with R_4 to form a ring containing the N atom to which both are joined, and when m is 1-6 and n is 0, R_1 and R_3 are absent, and R_2 and R_4 are hydrocarbon groups, and when both m and n are at least 1, R_2 and R_4 are absent; and when z is 2, m and n are 0, R_1 and R_3 are hydrocarbon groups and R_2 and R^4 are absent.

Particularly useful linear tertiary polyamines within the aforesaid description are 2,4-dimethyl-2,4-diazapentane, 2,5-dimethyl-2,5-diazahexane, 1,1'-(1,2-ethanediyl)bis[piperidine], N,N,N',N'-tetramethyl-1,2-diaminocyclohexane, 1,4-dimethyl-1,4-diazacyclohexane, diazabicyclo[2.2.2]octane, 2,6-dimethyl-2,6-diazaheptane, 2,7-dimethyl-2,7-diazaoctane, 2,7-dimethyl-2,7-diaza-4-octene, 2,7-dimethyl-2,7-diaza-4-octyne, 2,9-dimethyl-2,9-diazadecane, and 2,5,8,11-tetramethyl-2,5,8,11-tetraazadodecane. Among these compounds, diazabicyclo[2.2.2]-octane, 2,6-dimethyl-2,6-diazaheptane, 2,7-dimethyl-2,7-diazaoctane, and 2,5,8,11-tetramethyl-2,5,8,11-tetrazadecane are preferred, and diazabicyclo[2.2.2]octane is especially attractive.

Macrocyclic tertiary polyamines such as 1, 4, 8, 11-tetraazacyclotetradecane, for example, are also useful, as are sparteine and hexamethylenetetraamine.

Although other acid salts are effective, it is preferred that the salt be a hydrohalide, especially a hydrochloride. Acid salts of tertiary amines which may be employed in this invention include, for example, diazabicyclo[2.2.2]octane dihydrochloride, 2,7-dimethyl-2,7-diazaoctane dihydrochloride, 2,3,4,6,7,8,9,10-octahydropyrimido[1,2-a]azepine hydrochloride, and quinuclidine hydrochloride.

The process of this invention is carried out between approximately equimolar amounts of the acyl halide, preferably the acyl chloride, aldehyde and aqueous solution of cyanide salt in the water-immiscible aprotic solvent, but slight excesses of the acyl halide and cyanide salt are typically used. The acyl halide may be added last, preferably dropwise, to the stirred reaction mixture, but it is preferred to add a solution containing aldehyde and acyl halide to a stirred mixture of aqueous cyanide salt and water-immiscible aprotic solvent. Although the reaction can be carried out over a wide temperature range, the range 0°C-50°C is satisfactory in most cases, and it is preferred to carry out the reaction at room temperature, since neither external heating nor cooling are then required.

The process will be understood more readily by reference to the following Examples, which illustrate it. Temperatures are in degrees Celsius. The reactions exemplified were, in many cases, monitored by gas liquid partition chromatography (glpc), and the time required for disappearance of the limiting reagent after beginning addition of the acyl halide was determined, together with the amount of alpha-cyano ester produced at that time.

Example 1

Preparation of α-cyano-3-phenoxybenzyl 3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropanecarboxylate

A. Using diazabicyclo[2.2.2]octane

(1) A flask was charged with 3-phenoxybenzaldehyde (1.98 g, 10.0 mmole), sodium cyanide (0.59 g, 12 mmole), 20 ml n-heptane, 1 ml water, and diazabicyclo[2.2.2]-octane (0.022 g, 0.2 mmole). This mixture was vigorously stirred, and 3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropanecarbonyl chloride (2.38 g, 10.5 mmole) was added in one portion. Stirring was continued at room temperature for one hour, at which time glpc indicated a 94% yield of the desired alpha-cyano ester. The

mixture was filtered. The filter cake was washed twice with 10 ml portions of diethyl ether. The filtrate was dried over magnesium sulfate, and the heptane was stripped under reduced pressure to yield the desired ester as a residual oil (4.10 g).

Use of the optically active (1R,cis) carbonyl chloride in the aforesaid process afforded the corresponding optically active ester in 96% yield within 1 hr. reaction time.

(2) Under a dry nitrogen atmosphere a mixture of sodium cyanide (5.9 g, 0.12 mole) and 1,4-diazabicyclo-[2.2.2]octane (0.22 g, 0.002 mole) in 10 grams of water was stirred at room temperature. During a one hour period a solution of 3-phenoxybenzaldehyde (20.6 g, 0.1 mole) and 3-(2,2-dichloroethenyl)-2, 2-dimethylcyclopropanecarbonyl chloride (24.1 g, 0.105 mole) in 120 ml of n-octane was added to the reaction mixture. After complete addition, the reaction mixture was stirred for one hour. An aqueous solution containing 20% sodium carbonate was added to the reaction mixture and the total warmed to 60°. The organic phase was separated and washed with water, dried over anhydrous magnesium sulfate and filtered. The solvent was removed from the filtrate under reduced pressure to yield α-cyano-3-phenoxybenzyl 3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropanecarboxylate.

B. Using 2,6-dimethyl-2,6-diazaheptane

A flask was charged with a solution of 3-phenoxybenzaldehyde (1.98 g, 10 mmole) in 10 ml n-heptane. This solution was cooled to 10°, then 2,6-dimethyl-2,6-diazaheptane (26 mg, 0.2 mmole), sodium cyanide (0.59 g, 12 mmole), and 1 ml water were added. 3-(2,2-Dichloroethenyl)-2,2-dimethylcyclopropanecarbonyl chloride (2.38 g, 10.5 mmole) was then added in one portion with stirring, and the temperature of the reaction mixture was maintained at 8-12°. After 45 minutes, glpc indicated a 93% yield of the desired alpha-cyano ester.

After a total of 1.25 hours, the reaction mixture was filtered. The filter cake was washed with ether, and the solvent was evaporated from the filtrate, affording the desired ester (4.3 g).

C. Using 2,5,8,11-tetramethyl-2,5,8,11-tetraazadodecane

A flask equipped with a stirrer, addition funnel, and an inlet for nitrogen gas was charged with sodium cyanide (0.59 g, 0.012 mole) dissolved in 1 ml water, 2,5,8,11-tetramethyl-2,5,8,11-tetraazadodecane (0.048 g, 0.2 mmole) in 3 ml heptane, and 3-phenoxybenzaldehyde (1.98 g, 0.01 mole) in 7 ml heptane. The reactants were mixed under a nitrogen atmosphere. 3-(2,2-Dichloroethenyl)-2,2-dimethylcyclopropanecarbonyl chloride (2.38 g, 0.0105 mole) in 10 ml heptane was added dropwise to the stirred mixture over a period of 20 minutes. Twenty minutes later, a total of 40 minutes, glpc indicated a 93% yield of the desired ester. The reaction mixture was stirred for another 40 minutes, then poured into a separatory funnel, diluted with 40 ml diethyl ether, washed once with a 1N aqueous solution of sodium hydroxide, three times with water, and once with saturated aqueous sodium chloride solution. After phase separation, the separated ethereal layer was dried over magnesium sulfate, and the solvent was evaporated, affording the ester as a pale yellow oil (4.02 g).

D. Using 4,7,13,16,21-pentaoxa-1,10-diazabicyclo-[8.8.5]tricosane

A flask was charged with 3-phenoxybenzaldehyde (1.98 g, 10 mmole), 10 ml n-heptane, 4,7,13,16,21-pentaoxa-1,10-diazabicyclo[8.8.5]tricosane (66 mg, 0.2 mmole), sodium cyanide (0.59 g, 12 mmole), 1 ml water, and a solution of 3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropanecarbonyl chloride (2.38 g, 10.5 mmole) in 10 ml n-heptane. The reaction mixture was stirred, and an exotherm (to approximately 40°) was observed after 20 minutes. After 50 minutes, glpc showed a 99% yield of

the desired ester. The reaction mixture was filtered, diluted with ether, dried over magnesium sulfate, and the solvent was evaporated to afford the desired ester (3.90 g).

E. Using Tetramethylethylene Diamine

A solution of 3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropanecarbonyl chloride (114 g, 0.315 mole) and 3-phenoxybenzaldehyde (61.9 g, 0.3 mole) in 275 ml of n-heptane was added dropwise under nitrogen in one hour to a stirred mixture of sodium cyanide (18 g, 0.36 mole), tetramethylethylene diamine (0.7 g, 0.006 mole), and 30 g of water at about 40°. After the addition, the reaction mixture was stirred for 90 minutes at about 40°. The reaction mixture was worked up as in Example 1A.(2), producing the desired ester.

F. Using Tetramethyl-1,6-hexane Diamine

By the method of Example 1E. above, but substituting tetramethyl-1,6-hexane diamine for tetramethylethylene diamine, α-cyano-3-phenoxybenzyl 3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropanecarboxylate was prepared.

The preparation of α-cyano-3-phenoxybenzyl 3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropanecarboxylate using other tertiary amine or polyamine and cryptate rate-promoting agents under otherwise similar conditions gave the results shown in Table 1.

Example 2

Preparation of α-cyano-3-phenoxybenzyl 3-(2,2-dibromoethenyl)-2,2-dimethylcyclopropanecarboxylate using diazabicyclo[2.2.2]octane

A flask was charged with 3-phenoxybenzaldehyde (1.98 g, 10.0 mmole), 10 ml n-heptane, diazabicyclo-[2.2.2]octane (22 ml, 0.2 mmole), sodium cyanide (0.59 g, 12 mmole), and 1 ml water. 3-(2,2-Dibromoethenyl)-2,2-dimethylcyclopropanecarbonyl chloride (3.32 g, 10.5 mmole) in 10 ml n-heptane was added with stirring. After 2 hours, the reaction mixture was filtered, the filter cake was washed with 30 ml of ether, and the

filtrate was dried over magnesium sulfate. The solvent was stripped, affording the desired ester as a yellow oil (4.4 g, 96% yield).

Example 3

Preparation of α-cyano-3-phenoxybenzyl 3-(2-chloro-3,3,3-trifluoropropenyl)-2,2-dimethylcyclopropanecarboxylate using 2,7-dimethyl-2,7-diazaoctane

A flask was charged with 3-phenoxybenzaldehyde (1.98 g, 10 mmole), 10 ml n-heptane, 2,7-dimethyl-2,7-diazaoctane (29 mg, 0.2 mmole), sodium cyanide (0.59 g, 12 mmole) and 1 ml water. 3-(2-Chloro-3,3,3-trifluoropropenyl)-2,2-dimethylcyclopropanecarbonyl chloride (2.0 g, 10.5 mmole) dissolved in 10 ml n-heptane was then added in one portion. After 1.3 hr., the conversion was complete. The reaction mixture was stirred for 4.5 hr, when 5 ml diethyl ether and 5 ml 1N aqueous sodium hydroxide solution were added. The resultant mixture was stirred for 1.5 hr and the two phases separated. The organic phase was washed once with 1N aqueous sodium hydroxide solution, once with water, and once with a saturated aqueous sodium chloride solution, then dried over magnesium sulfate, filtered, and the solvent distilled off under reduced pressure to afford the desired ester (4.1 g, 91% yield).

Example 4

Preparation of α-cyano-3-phenoxybenzyl 2,2,3,3-tetramethylcyclopropanecarboxylate using 2,6-dimethyl-2,6-diazaheptane

A flask was charged with 3-phenoxybenzaldehyde (3.16 g, 16 mmole), 10 ml n-heptane, 2,6-dimethyl-2,6-diazaheptane (26 mg, 0.2 mmole), sodium cyanide (0.94 g, 19.2 mmole) and 1 ml water. 2,2,3,3-Tetramethylcyclopropanecarbonyl chloride (2.6 g, 16.7 mmole) dissolved in 10 ml n-heptane was added next, in one portion. An exotherm (to approximately 38°) was observed upon addition of the acid chloride. Analysis indicated a 74% yield of the desired ester in 4 hours. After

cooling, the reaction mixture was filtered, diluted with diethyl ether, dried over magnesium sulfate, and distilled under reduced pressure to afford an orange residual oil. The oil was dissolved in 25 ml diethyl ether, and the resultant ethereal solution was mixed for 2 hr with a 1N aqueous sodium hydroxide solution. After phase separation, the ethereal layer was washed once with water, once with a saturated aqueous sodium chloride solution, dried over magnesium sulfate, and the solvent was distilled under reduced pressure to afford the desired ester (3.0 g).

Example 5

Preparation of α-cyano-3-phenoxybenzyl 2-(4-chlorophenyl)-3-methyl butanoate

A. Using diazabicyclo[2.2.2]octane

A flask was charged with 3-phenoxybenzaldehyde (1.98 g, 10 mmole), 10 ml n-heptane, diazabicyclo[2.2.2]-octane (22 mg, 0.2 mmole), sodium cyanide (0.59 g, 12 mmole), and 1 ml water, and stirring was begun. 2-(4-Chlorophenyl)-3-methylbutanoyl chloride (2.42 g, 10.5 mmole) in 10 ml n-heptane was then added in one portion. The reaction mixture was stirred at room temperature for 1 hr at which time glpc indicated a 74% yield of the desired ester. Stirring was continued overnight, then the reaction mixture was filtered, diluted with diethyl ether, and the solvent was distilled under reduced pressure to afford the desired ester as the residue (4.02 g).

B. Using 2,5,8,11-tetramethyl-2,5,8,11-tetraazadodecane

A flask was charged with 3-phenoxybenzaldehyde (1.98 g, 10 mmole), 20 ml n-heptane, 2,5,8,11-tetramethyl-2,5,8,11-tetraazadodecane (0.046 g), sodium cyanide (0.59 g, 12 mmole), and 1 ml. water. With stirring, 2-(4-chlorophenyl)-3-methylbutanoyl chloride (2.42 g, 10.5 mmole) was added dropwise over a period of 6 minutes. The reaction mixture was stirred at room

temperature. Analysis by glpc 2.4 hr. after the acyl chloride had been added indicated a 67.7% yield of the desired ester. Stirring was continued overnight, and the desired ester (3.4 g) was isolated as described in the preceding Example.

Example 6

Preparation of α-cyano-3-phenoxybenzyl 3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropanecarboxylate

A. Using 1,4-piperazinebisethanesulfonic acid as the rate-promoting agent

A flask was charged with 3-phenoxybenzaldehyde (1.98 g, 10 mmole), 10 ml n-heptane, 1,4-piperazinebisethanesulfonic acid (60 mg, 0.2 mmole), sodium cyanide (0.59 g, 12 mmole), 1 ml water, and a solution of 3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropanecarbonyl chloride (2.38 g, 10.5 mmole) in 10 ml n-heptane. The reaction mixture was stirred for 4.5 hours (glpc indicated a 91% yield after 1 hr, 50 min), diluted with 30 ml diethyl ether, then washed once with 1N aqueous sodium hydroxide solution (20 ml), once with water (20 ml), and once with a saturated aqueous sodium chloride solution (20 ml). After separation, the clear yellow ethereal solution was dried over magnesium sulfate; then the solvent was evaporated to afford the desired ester (4.05 g).

B. Using 3-(cyclohexylamino)propanesulfonic acid as the rate-promoting agent

(1) In the manner of Example A above, but substituting 3-(cyclohexylamino)propanesulfonic acid (44 mg, 0.2 mmole) for the 1,4-piperazinebisethanesulfonic acid, glpc indicated a 97.2% yield of the desired ester after 95 minutes and isolation afforded the desired ester (3.49 g).

In a similar experiment, glpc indicated a 99% yield of the desired ester in two hours.

(2) A stirred mixture of sodium cyanide (18.0 g, 0.36 mole) and 3-(cyclohexylamino)propanesulfonic acid (1.34 g, 0.006 mole) in 300 ml of water was warmed to

40°. During a one hour period, maintaining a reaction temperature of about 40°, a solution of cis-3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropanecarbonyl chloride (71.7 g, 0.315 mole) and 3-phenoxybenzaldehyde (61.9 g, 0.3 mole) in 262.2 g of n-heptane was added. The mixture was then stirred at 40° for one additional hour, after which it was washed with an aqueous solution containing 20% sodium carbonate and then with water. The organic phase was separated from the mixture and the solvent removed by distillation under reduced pressure to give α-cyano-3-phenoxybenzyl cis-3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropanecarboxylate.

The substitution of other rate-promoting agents under otherwise similar conditions gave the following yields (glpc) after the indicated reaction times.

Rate-Promoting Agent	Reaction Time	Yield
2-[4-(2-hydroxyethyl)piperazine-1-yl]ethanesulfonic acid	55 min.	91%
4-pyridineethanesulfonic acid	2.3 hr.	94%
2-[N,N-di-(2-hydroxy)ethyl]aminoethanesulfonic acid	3.3 hr.	90%

Example 7

Preparation of α-cyano-3-phenoxybenzyl 2-(4-chlorophenyl)-3-methyl butanoate using 3-(cyclohexylamino)propanesulfonic acid as the rate-promoting agent

A flask was charged with 3-(cyclohexylamino)propanesulfonic acid (42 mg), 3-phenoxybenzaldehyde (1.90 g, 9.6 mmole), sodium cyanide (0.56 g, 12 mmole), 1 ml water, and 15 ml n-heptane. 2-(4-Chlorophenyl)-3-methylbutanoyl chloride (2.34 g, 10.1 mmole) in 5 ml n-heptane was added dropwise over a period of 24 minutes to the stirred mixture. Thirty minutes after the addition was complete, a total of 54 minutes, glpc indicated a 95.6% yield of the desired ester. After stirring overnight, the reaction mixture was filtered and extracted with

ether. The ether was evaporated from the extract, affording α-cyano-3-phenoxybenzyl 2-(4-chlorophenyl)-3-methyl butanoate (3.47 g).

Example 8

Preparation of α-cyano-3-phenoxybenzyl 3-(2,2-dichloroethenyl)2,2-dimethylcyclopropanecarboxylate using diazabicyclo[2.2.2]octane dihydrochloride as the rate-promoting agent

(1) A flask was charged with 3-phenoxybenzaldehyde (1.98 g, 10.0 mmole) 10 ml n-heptane, diazabicyclo[2.2.2]-octane dihydrochloride (30 mg, 0.2 mmole), sodium cyanide (0.59 g, 12 mmole), 1 ml water, and a solution of 3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropanecarbonyl chloride (2.38 g, 10.5 mmole) in 10 ml n-heptane. The reaction mixture was stirred, and after 1.5 hours glpc indicated a 96% yield of the desired ester. After a total of 1 hr., 50 min, the reaction mixture was filtered, diluted with ether, the phases were separated, the ether phase was dried over magnesium sulfate, and the solvent was evaporated to afford the desired ester (3.98 g).

(2) A stirred mixture of sodium cyanide (18.1 g, 0.36 mole) and diazabicyclo[2.2.2]octane dihydrochloride (1.11 g, 0.006 mole) in 30 g of water was warmed to 40°. During a one hour period a solution of 3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropanecarbonyl chloride (77.6 g, 0.33 mole) and 3-phenoxybenzaldehyde (61.5 g, 0.3 mole) in 102 ml of n-heptane was added to the reaction mixture. After complete addition, the reaction mixture was stirred for 40 minutes and an additional 3.5 g (0.015 mole) of the acyl chloride added. The reaction mixture was stirred for an additional 40 minutes and then washed with 100 g of a 10% aqueous sodium carbonate solution and then water. The organic phase was separated from the mixture and the solvent removed by distillation under reduced pressure to give α-cyano-3-phenoxybenzyl 3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropanecarboxylate.

The preparation of α-cyano-3-phenoxybenzyl 3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropanecarboxylate using other rate-promoting agents under otherwise similar conditions gave the following results.

Rate-Promoting Agent	Reaction Time	Yield
2,7-dimethyl-2,7-diazaoctane dihydrochloride	1.4 hr	96%
2,3,4,6,7,8,10-octahydropyrimido[1,2-a]azepine hydrochloride	4 hr	99%
quinuclidine hydrochloride	1.8 hr	98%

Table 1

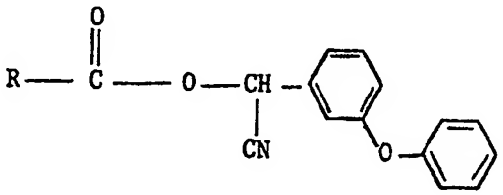
PREPARATION OF α-CYANO-3-PHENOXYBENZYL 3-(2,2-DICHLOROETHENYL)-2,2-DIMETHYLCYCLOPROPANECARBOXYLATE USING OTHER TERTIARY AMINE OR POLYAMINE AND CRYPTATE RATE-PROMOTING AGENTS

Rate-Promoting Agent	Reaction Time	Yield
tri-n-hexylamine	4.5 hours	82%
triethylamine	2 hours	89%
2,4-dimethyl-2,4-diazapentane	24 hours	96%
2,5-dimethyl-2,5-diazahexane	0.5 hour	91%
2,9-dimethyl-2,9-diazadecane	1.0 hour	96%
1,1'-(1,2-ethanediyl)-bis[piperidine]	1.0 hour	94%
1,4-dimethyl-1,4-diazacyclohexane	1.0 hour	86%
N,N,N',N'-tetramethyl-1,2-diaminocyclohexane	1.5 hours	96%
1,4,8,11-tetramethyl-1,4,8,11-tetraazacyclotetradecane	1.5 hours	96%
(-)-sparteine	1.3 hours	95%

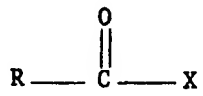
Claims:

1. A process to prepare an alpha-cyano ester characterized by reacting an acyl halide with an aldehyde in a mixture of substantially water-immiscible aprotic solvent and an aqueous solution of water-soluble cyanide salt in the presence of a catalytic amount of rate-promoting agent selected from tertiary amines or polyamines, cryptates, amphoteric surfactants, and acid salts of tertiary amines.

2. A process according to claim 1 characterized in that an insecticidal α-cyano-3-phenoxybenzyl ester of the formula

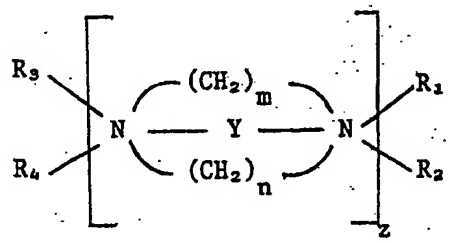


wherein R is selected from 3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropyl, 3-(2,2-dibromoethenyl)-2,2-dimethylcyclopropyl, 3-(2-chloro-3,3,3-trifluoropropenyl)-2,2-dimethylcyclopropyl, 2,2,3,3-tetramethylcyclopropyl, and 1-(4-chlorophenyl)-2-methylpropyl is prepared by reacting an acyl halide of the formula



wherein X is chlorine or bromine and R is as defined above with 3-phenoxybenzaldehyde in a mixture of substantially water-immiscible aprotic solvent and an aqueous solution of water-soluble cyanide salt in the presence of a catalytic amount of amphoteric surfactant rate-promoting agent selected from tertiary amines or polyamines, cryptates, amphoteric surfactants selected from aminoalkylsulfonic acids, and acid salts of tertiary amines.

3. A process according to claim 2 characterized by using a rate-promoting agent selected from tertiary polyamines which are linear tertiary polyamines of the formula



wherein Y is $-(CH_2)_k-$ with k being 1-6, C_3-C_7 cycloalkane, C_2-C_6 alkenyl, or C_2-C_6 alkynyl; z is 1 or 2, and when z is 1, m and n are 0 or independently 1-6, and when m and n are 0, R_1, R_2, R_3, and R_4 are hydrocarbon groups, and R_1 may be joined with R_2, and R_3 may be joined with R_4 to form a ring containing the N atom to which both are joined, and when m is 1-6 and n is 0, R_1 and R_3 are absent, and R_2 and R_4 are hydrocarbon groups, and when both m and n are at least 1, R_2 and R_4 are absent; and when z is 2, m and n are 0, R_1 and R_3 are hydrocarbon groups and R_2 and R_4 are absent, 1,4,8,11-tetramethyl-1,4, 8,11-tetraazacyclotetradecane, sparteine, and cryptates.

4. The process of claim 3 characterized in that the linear tertiary polyamine is selected from 2,4-dimethyl-2,4-diazapentane, 2,5-dimethyl-2,5-diazahexane, 1,1'-(1,2-ethanediyl)-bis[piperidine], N,N,N',N'-tetramethyl-1,2-diaminocyclohexane, 1,4-dimethyl-1,4-diazacyclohexane, diazabicyclo[2.2.2]octane, 2,6-dimethyl-2,6-diazaheptane, 2,7-dimethyl-2,7-diazaoctane, 2,9-dimethyl-2,9-diazadecane, and 2,5,8,11-tetramethyl-2,5,8,11-tetraazadodecane.

5. The process of claim 4 characterized in that the linear tertiary polyamine is diazabicyclo[2.2.2]-octane, 2,6-dimethyl-2,6-diazaheptane, 2,7-dimethyl-2,7-

The process of this invention is especially effective in producing a high yield of insecticidal α-cyano-3-phenoxybenzyl esters in a short time when the rate-promoting agent is a tertiary polyamine or cryptate and R is 3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropyl, 3-(2,2-dibromoethenyl)-2,2-dimethylcyclopropyl, or 3-(2-chloro-3,3,3-trifluoropropenyl)-2,2-dimethylcyclopropyl, or when the rate-promoting agent is an amphoteric surfactant selected from aminoalkylsulfonic acids and R is 3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropyl or 1-(4-chlorophenyl)-2-methylpropyl, or when the rate-promoting agent is an acid salt of a tertiary amine and R is 3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropyl, 3-(2,2-dibromoethenyl)-2,2-dimethylcyclopropyl, or 3-(2-chloro-3,3,3-trifluoropropenyl)-2,2-dimethylcyclopropyl. Outstanding results are obtained when R is 3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropyl.

Although the process of this invention is especially advantageous when R is selected from the groups named above, the process is also effective in producing other alpha-cyano esters wherein R is an aliphatic or aromatic group, which may optionally contain various substituents. Although the process of this invention is preferably employed to produce α-cyano-3-phenoxybenzyl esters by using 3-phenoxybenzaldehyde as a reactant, the process is equally suited to the production of other alpha-cyano esters by varying the type of aldehyde employed in the process.

Various aprotic solvents which are substantially water-immiscible may be used in the process. Any alkyl, haloalkyl, aryl, haloaryl, aralkyl, haloaralkyl, or cyclic hydrocarbon, provided that it is a liquid at temperatures between about 0°C and 50°C and forms a discrete second phase when mixed with water, may be used. Such solvents include iso-hexane, 3-methylpentane, 2,3-dimethylbutane, 2,2-dimethylbutane, n-heptane, n-octane, petroleum ether, ligroin, n-propyl bromide,

n-propyl iodide, n-butyl chloride, n-butyl bromide, n-pentyl chloride, n-pentyl bromide, diethyl ether, dipropyl ether, dibutyl ether, benzene, toluene, and xylene, for example. Among these solvents, n-heptane is preferred because it is readily available and inexpensive.

A number of water-soluble cyanide salts may be used; for example, the salt may be an alkali metal cyanide such as lithium, sodium, potassium, rubidium, or cesium cyanide, or mixtures thereof. Among these, sodium cyanide generally is preferred. However, when it is desired to use certain cryptates as rate-promoting agents, it may be desirable to substitute lithium or potassium cyanide as described below.

The cyanide salt is dissolved in water, the amount of water employed being relatively small, but preferably sufficient to keep all of the cyanide salt in solution under the reaction conditions. In the case that the salt is sodium cyanide, the preferred molar ratio of water to sodium cyanide is between about 3.5 and 6, preferably about 4.5.

The process of this invention is conducted in the presence of a catalytic amount of rate-promoting agent selected from tertiary amines, polyamines, cryptates, amphoteric surfactants, and acid salts of tertiary amines. For purposes of this invention, a catalytic amount of rate-promoting agent is in the range 1-5 mole percent based on aldehyde, advantageously about 2 mole percent.

The rate-promoting agent may be a tertiary amine or polyamine, a tertiary polyamine being a compound containing more than one tertiary amino nitrogen atom. Particularly desirable tertiary polyamines are linear tertiary polyamines of the formula

are at least 1, R_2 and R_4 are absent; and when z is 2, m and n are 0, R_1 and R_3 are hydrocarbon groups and R_2 and R^4 are absent.

20. The process of claim 19 characterized in that the rate-promoting agent is selected from diazabicyclo-[2.2.2]octane dihydrochloride, 2,7-dimethyl-2,7-diaza-octane dihydrochloride, 2,3,4, 6,7,8,9,10-octahydropyri-mido[1,2-a]azepine hydrochloride, and quinuclidine hydrochloride.

21. The process of claim 20 characterized in that the rate-promoting agent is diazabicyclo[2.2.2]octane dihydrochloride.

22. A process according to any one of claims 19-21 characterized in that R is 3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropyl.

23. A process according to any one of claims 19-21 characterized in that the water-immiscible aprotic solvent is n-heptane.

24. A process according to any one of claims 19-21 characterized in that the water-soluble cyanide salt is sodium cyanide.

European Patent Office

EUROPEAN SEARCH REPORT

Application number

EP 80 20 0905.0

DOCUMENTS CONSIDERED TO BE RELEVANT			CLASSIFICATION OF THE APPLICATION (Int. Cl.³)
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	
X	DE - A1 - 2 825 197 (SUMITOMO CHEMICAL) * claim 11; page 16, line 20 to page 17, line 3 * --	1,2	C 07 C 120/00 C 07 C 121/66 C 07 C 121/75
	EP - A1 - 0 002 288 (SHELL INTERNATIONALE RESEARCH MAATSCHAPPIJ B.V.) * claims 1 to 5 * --	1,2	
P	E.V. DEHMLOW et al. "Phase Transfer Catalysis" 1980, VERLAG CHEMIE, Weinheim * pages 46 to 52 * ----	1,2	C 07 C 120/00 C 07 C 121/00

TECHNICAL FIELDS SEARCHED (Int. Cl.³)

CATEGORY OF CITED DOCUMENTS

X: particularly relevant
A: technological background
O: non-written disclosure
P: intermediate document
T: theory or principle underlying the invention
E: conflicting application
D: document cited in the application
L: citation for other reasons

&: member of the same patent family, corresponding document

X The present search report has been drawn up for all claims

Place of search	Date of completion of the search	Examiner
Berlin	16-12-1980	STOOS

EPO Form 1503.1 06.78